Risk Evaluation and Mitigation Strategy (REMS)

Enbrel® (etanercept)

BLA 103795

Report Prepared by:

Immunex Corp, a wholly-owned subsidiary of Amgen Inc.
One Amgen Center Drive
Thousand Oaks, CA 91320-1799
805-447-1000

REMS – Histoplasmosis

I. Goals

To communicate and mitigate the risks associated with Enbrel® (etanercept) therapy by:

- Alerting and warning healthcare providers about unrecognized histoplasmosis and other invasive fungal infections associated with tumor necrosis factor (TNF) blocker use.
- Educating patients about the serious risks associated with Enbrel therapy.

II. REMS Elements

A. Medication Guide

Enbrel is packaged for individual use with the United States Prescribing Information, Medication Guide, and Patient Instructions for Use inside a sealed carton.

Because the Medication Guide is included inside the Enbrel carton, Amgen has met the sponsor requirements of 21 CFR 208.24 for distribution of the Medication Guide.

Please see the Medication Guide in Appendix 1.

B. Communication Plan

The following communication plan will be implemented within 60 days after the approval of the REMS containing the communication plan.

In accordance to FDCA 505-1(e)(3), Amgen will implement a communication plan targeted to healthcare professionals, including rheumatologists, dermatologists, and internal medicine and family medicine physicians to support implementation of this REMS.

The communication plan will convey the following information:

- the risk of developing invasive fungal infections, including histoplasmosis, coccidioidomycosis, blastomycosis, and other opportunistic fungal infections while being treated with TNF blockers;
- descriptive information on the signs and symptoms of fungal infections including histoplasmosis; and
- references and background information regarding the treatment of these infections.

The purpose of the communication plan is to establish the REMS in the healthcare community and communicate new safety information. This element of the REMS is not intended to continue over the lifetime of the product; it will function only to disseminate the new safety information about histoplasmosis and other invasive fungal infections associated with TNF blocker use. The healthcare provider-directed communication plan will consist of the following tools.

- "Dear Healthcare Provider" Letter (DHCP) – provides information to the HCP regarding the risks of developing histoplasmosis and other invasive fungal infections associated with the use of TNF blockers as well as the signs and symptoms of these infections (Appendix 2).

  The DHCP letter will be disseminated to US healthcare providers in the following specialties:

  - rheumatologists (adult and pediatric);
  - dermatologists;
  - internal medicine and family medicine physicians who have prescribed Enbrel within the last 12 months, as reflected by IMS Health Inc prescription data
  - infectious disease and emergency room physicians.
- Scientific Education Slide Deck – provides information about the occurrence of unrecognized histoplasmosis and other invasive fungal infections in patients being treated with TNF inhibitors; the slide deck will be presented to rheumatology and dermatology specialists (Appendix 3); and
- REMS-dedicated Webpage linked from Enbrel.com – provides a link to a separate webpage dedicated to the REMS program, which will contain the "Dear Healthcare Provider" Letter, the scientific education slide deck, and the Medication Guide (Appendix 4). The REMS webpage will be available to all healthcare providers as it is in the public domain.

III. Elements to Assure Safe Use

The REMS does not include any Elements to Assure Safe Use.

IV. Implementation System

An implementation system is not a required component of the proposed REMS because there are no elements to assure safe use.

V. Timetable for Assessments of the REMS

Amgen will submit REMS assessments to FDA 18 months, 28 months, 3 years, and 7 years from the date of the initial approval of the REMS.

To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Amgen will submit each assessment so it will be received by the FDA on or before the due date.